Group I is claims 1-8, 16-21, 25-26, 40-41, 49, 57, 65, 73, 84, and 92, drawn to a method for treatment of pulmonary airway disease in a subject suffering from pulmonary airway disease comprising administering a therapeutic amount of a β-adrenergic inverse agonist to the subject to treat the pulmonary disease, and a therapeutically effective amount of an additional agent selected from the group consisting of a β_2-selective adrenergic agonist, a steroid, an anticholinergic drug, a xanthine compound, an anti-IgE antibody, a leukotriene modifier, and a phosphodiesterase inhibitor in order to treat the pulmonary airway disease, classified in Class 424, various subclasses; and

Group II is claims 27 and 99, drawn to a pharmaceutical composition comprising: (a) nadolol in a quantity selected from the group consisting of 1 mg, 3 mg, 5 mg, 10 mg, 15 mg, 30 mg, 50 mg, and 70 mg, and a pharmaceutically acceptable carrier; or comprising: (b) (i) a therapeutically effective amount of a β-adrenergic inverse agonist; (ii) a therapeutically effective amount of a second therapeutic agent effective to treat a pulmonary airway disease, the second therapeutic agent being selected from the group consisting of β_2-selective adrenergic agonist, a steroid, an anticholinergic drug, a xanthine compound, an anti-IgE antibody, a leukotriene modifier, and a phosphodiesterase inhibitor; and (iii) a pharmaceutically acceptable carrier, classified in Class 424, various subclasses.

The Restriction Requirement stated that the inventions were distinct, each from the other, for the following reasons:

The inventions of Group I are directed to related processes. The related inventions are distinct if the (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed can have a materially different design, mode of operation, function, or effect. The process for forming each of the products in the groups, form different products and start with different compounds. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

Group II is directed to related products. The related inventions are distinct if the (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed can have a materially different design, mode of operation, function, or effect. In the instant case, the structures in each group differ in chemical structure, reactivity and use. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

Groups I and II, and permutations thereof, are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, analogs of cedax (ceftibuten) can be used for treating pulmonary or respiratory disease.

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention; and

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. § 101 and/or 35 U.S.C. § 112, first paragraph.

The Examiner has required restriction between product and process claims. Where Applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 C.F.R. § 1.104. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. Further, note that the prohibition against double patenting rejections of 35 U.S.C. § 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues.

II. THE REQUIREMENT FOR ELECTION OF SPECIES

The Requirement for Election of Species stated that the above-identified application contained claims directed to the following species that were considered patentably distinct: the species recited in claims 2, 4-5, 7, 16, 18, 40-41, 49, 57, 65, 84, and 92.

Although the Requirement for Election of Species did not specifically recite the species, the species recited in these claims are as follows:

(1) For claim 2: β_2-selective inverse agonists and non-selective inverse agonists having inverse agonist activity against both β_1 and β_2-adrenergic receptors.

(2) For claim 4: nadolol, bupranolol, butoxamine, carazolol, carvedilol, ICI-118,551, levobunolol, metoprolol, propranolol, sotalol, timolol, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

(3) For claim 5: nadolol and analogues of nadolol of Formula (I).

(4) For claim 7: carvedilol and analogues of carvedilol of Formula II.

(5) For claim 16: oral, sustained-release oral, parenteral, sublingual, buccal, insufflation, and inhalation as a route of administration.

(6) For claim 18: asthma, bronchiectasis, bronchitis, chronic obstructive pulmonary disease, Churg-Strauss syndrome, pulmonary sequelae of cystic fibrosis, emphysema, allergic rhinitis, and pneumonia as a pulmonary airway disease.

(7) For claim 40: a β_2-selective adrenergic agonist, a steroid, an anticholinergic drug, a xanthine compound, an anti-IgE antibody, a leukotriene modifier, and a phosphodiesterase inhibitor as an additional agent.

(8) For claim 41: albuterol, bitolterol, clenbuterol, clorprenaline, dobutamine, fenoterol, formoterol, isoetharine, isoprenaline, levabuterol, mabuterol, metaproterenol, pirbuterol, ritodrine, salbutamol, salmeterol, terbutaline, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof, as the β_2-selective adrenergic agonist.

(9) For claim 49: beclomethasone, budenoside, ciclesonide, flunisolide, fluticasone, methylprednisolone, prednisolone, prednisone, triamcinolone, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof, as the steroid.

(10) For claim 57: ipratropium bromide, tiatropium bromide, oxitropium bromide, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof, as the anticholinergic drug.

(11) For claim 65: theophylline, extended-release theophylline, aminophylline, theobromine, enprofylline, diprophylline, isbufylline, choline theophyllinate, albifylline, arofylline, bamifylline, and caffeine as the xanthine compound.

(12) For claim 73: monoclonal antibodies and genetically engineered antibodies that are derived from a monoclonal antibody as anti-IgE antibodies.

(13) For claim 84: ibudilast, montelukast, pranlukast, zafirlukast, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof, as the leukotriene modifier.

(14) For claim 92: roflumilast, cilomilast, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof, as the phosphodiesterase IV inhibitor.

Applicant was required under 35 U.S.C. § 121 to elect a single disclosed species, or a single grouping of patentably indistinct species, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. However, no generic claims are identified in the Requirement for Election of Species.

The Requirement for Election of Species stated that there is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. § 101 and/or 35 U.S.C. § 112, first paragraph.

Upon the allowance of a generic claim, Applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR § 1.141.

No matter which group Applicants elect, Applicants are required to elect a single, specific chemical compound encompassed by the generic formula of the corresponding group (e.g., if Applicants elect Group I, any single specific compounds recited by claim 1 would constitute a proper species election); Note: Applicants should identify the elected compound using proper chemical nomenclature and provide the chemical structure.

III. RESPONSE TO RESTRICTION REQUIREMENT

Applicant elects the invention of Group I, claims 1-8, 16-21, 25-26, 40-41, 49, 57, 65, 73, 84, and 92, drawn to a method for treatment of pulmonary airway disease in a subject suffering from pulmonary airway disease comprising administering a therapeutic amount of a β-adrenergic inverse agonist to the subject to treat the pulmonary disease, and a therapeutically effective amount of an additional agent selected from the group consisting of a β_2-selective adrenergic agonist, a steroid, an anticholinergic drug, a xanthine compound, an anti-IgE antibody, a leukotriene modifier, and a phosphodiesterase inhibitor in order to treat the pulmonary airway disease, classified in Class 424, various subclasses, for prosecution on the merits, with traverse.

The Restriction Requirement is traversed for the following reasons:

Firstly, the Examiner has not met the burden for demonstrating the necessity for restriction. M.P.E.P. § 803 requires for restriction both: (1) that the inventions are independent or distinct as claimed; and (2) that there would exist a "serious burden" on the Examiner if all of the claims were examined in one application. These requirements have not been met.

In fact, the subject matter of Groups I and II as initially filed, claims 1-8, 16-21, 25-27, 40-41, 49, 57, 65, 73, 84, 92, and 99, are sufficiently related to avoid restriction, because there would be no "serious burden" on the Examiner if all of the claims were examined together in one application. The essence of the invention, from the standpoint of the imposition of a restriction requirement, is the discovery of the effectiveness of the use of β-adrenergic inverse agonists for the treatment of chronic pulmonary diseases and conditions, especially such diseases and conditions marked that are characterized by inflammation and airway hyperresponsiveness. No undue burden on the Examiner has in fact been demonstrated if all of these claims were examined in a single application.

Accordingly, the subject matter of the invention is sufficiently interrelated that no serious burden on the Examiner would exist if all the claims were examined on the merits. That is because the relevant art involved, if any relevant art exists, largely overlaps for these claims. For example, any publications, patents, or published patent applications describing the methods of Group I is also highly likely to describe the compositions employed in the methods, including any variants and any additional therapeutically active components employed. This statement is not to be taken as an admission that any such prior art exists, merely a statement that, should any relevant art exist, it is likely to be relevant to the subject matter of the inventions of Groups I and II.

Additionally, there is no evidence of record to support the Examiner's statement that restriction is proper because the inventions have acquired a separate status in the art in view of their different classification or that the inventions require a different field of search. In fact, the classifications are not stated as different.

Specifically, even if the classifications are different, the different classifications do not support a separate status in the art for the inventions of Groups I and II. The arguments above establish that there is no basis for claiming that a different field of search would be required or that the prior art applicable to the invention of Group I would not be applicable to the invention of Group II. Moreover, there is no evidence that any non-prior art issues exist under 35 U.S.C. § 101 and/or 35 U.S.C. § 112, first paragraph with respect to the inventions of Group I and Group II.

Applicant does not traverse the Restriction Requirement on the grounds of lack of patentable distinctness. Rather, Applicants traverse the Restriction Requirement on the grounds that the inventions of Groups I and are sufficiently related that restriction is not properly required, despite the possible existence of patentable distinctness.

Accordingly, the Restriction Requirement is respectfully traversed and the Examiner is respectfully requested to withdraw the Restriction Requirement and examine all pending claims on the merits.

IV. RESPONSE TO THE REQUIREMENT FOR ELECTION OF SPECIES

In response to the Requirement for the Election of Species, in view of the response to the Restriction Requirement and the election of the invention of Group I, Applicant makes the following elections, all with traverse:

(1) For claim 2, non-selective inverse agonists having inverse agonist activity against both β_1 and β_2-adrenergic receptors.

(2) For claim 4, nadolol as the β-adrenergic inverse agonist.

(3) For claim 5, nadolol as the β-adrenergic inverse agonist.

(4) For claim 7, carvedilol as the β-adrenergic inverse agonist.

(5) For claim 16, inhalation as a route of administration.

(6) For claim 18, chronic pulmonary obstructive disease as a pulmonary airway disease.

(7) For claims 40-41, salbutamol as the β_2-selective adrenergic agonist.

(8) For claim 49, prednisone as the steroid.

(9) For claim 57, ipratropium bromide as the anticholinergic compound

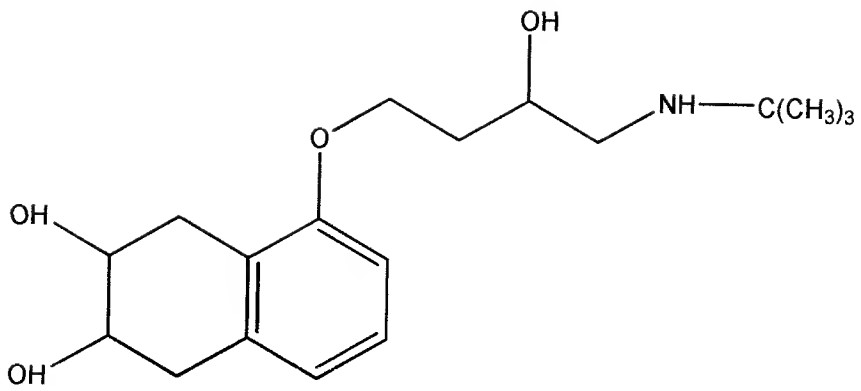
(10) For claim 65, theophylline as the xanthine compound.

(11) For claim 73, a monoclonal antibody as the anti-IgE antibody

(12) For claim 84, ibudilast as the leukotriene modifier.

(13) For claim 92, roflumilast as the phosphodiesterase IV inhibitor.

The single specific chemical compound whose election is required is nadolol, and the structure of nadolol is provided below:



Chemically, nadolol is (2*R*,3*S*)-5-{[(2*R*)-3-(*tert*-butylamino)-2-hydroxypropyl]oxy}-1,2,3,4-tetrahydronaphthalene-2,3-diol.

The following claims read on these individual species:

(1) For non-selective inverse agonists having inverse agonist activity against both β_1 and β_2-adrenergic receptors, claims 1-2, 4-8, 16-21, 25-26, 27, 40-41, 49-57, 65, 73, 84, 82, and 99, with claims 1-2, 4-8, 16-21, 25-26, 27, 40-41, 49-57, 65, 73, 84, 82, and 99 being generic with respect to the designation of the inverse agonist as a non-selective inverse agonist having inverse agonist activity against both β_1 and β_2-adrenergic receptors.

(2) For nadolol as the inverse agonist, claims 1-2, 4-6, 16-21, 25-26, 27, 40-41, 49, 57, 65, 73, 84, 92, and 99, with claims 1-2, 4-5, 16-21, 25-26, 40-41, 49, 57, 65, 73, 84, 92, and 99 being generic with respect to the designation of the inverse agonist as nadolol.

(3) For inhalation as the route of administration, claims 1-8, 16-21, 25-26, 27, 40-41, 49, 57, 65, 73, 84, 92, and 99, with all of these claims being generic with respect to the designation of the route of administration as inhalation.

(4) For chronic obstructive pulmonary disease as the pulmonary airway disease, 1-8, 16-21, 25-26, 27, 40-41, 49, 57, 65, 73, 84, 92, and 99, with all of these claims

being generic with respect to the designation of the pulmonary airway disease as chronic obstructive pulmonary disease.

(5) For salbutamol as the β_2-selective adrenergic agonist, claims 40-41, with claims 40-41 being generic with respect to the designation of the β_2-selective adrenergic agonist as salbutamol.

(6) For prednisone as the steroid, claim 49, with claim 49 being generic with respect to the designation of the steroid as prednisone.

(7) For ipratropium bromide as the anticholinergic drug, claim 57, with claim 57 being generic with respect to the designation of the anticholinergic drug as ipratropium bromide.

(8) For theophylline as the xanthine compound, claim 65, with claim 65 being generic with respect to the designation of the xanthine compound as theophylline.

(9) For a monoclonal antibody as the anti-IgE antibody, claim 73, with claim 73 being generic with respect to the designation of the anti-IgE antibody as a monoclonal antibody.

(10) For ibudilast as the leukotriene modifier, claim 84, with claim 84 being generic with respect to the designation of the leukotriene modifier as ibudilast.

(11) For roflumilast as the phosphodiesterase IV inhibitor, claim 92, with claim 92 being generic with respect to the designation of the phosphodiesterase IV inhibitor as roflumilast.

The Requirement for Election of Species is traversed on the following grounds:

The Requirement for Election is traversed on the grounds that the species of the invention recited in all of the pending claims are so closely related that there is no proper basis for requiring such an election. M.P.E.P. § 806.03 states: "Where the claims of an application define the same essential characteristics of a *single* disclosed embodiment of an invention, restriction therebetween should never be required. This is because the claims are but different definitions of the same disclosed subject matter, varying in breadth or scope of definition."

Here, the pending claims define the same essential characteristics of a single disclosed embodiment of the invention, as related to the inventive concept described above.

Moreover, as set forth above, many of the claims are generic with respect to the species as to which restriction is required, because these claims encompass not only that single species, but all possible alternative species between which restriction has been required. It is further submitted that these generic claims are allowable. The claims that are not directed solely to individual species (such as claim 6, directed specifically to the use of nadolol in the method) are properly linking claims under M.P.E.P. § 809. These are genus claims linking species claims. In fact, relatively few claims are properly considered species claims because of the presence of limitations that encompass all of the alternatives for the species described above.

Under M.P.E.P. § 809: "The linking claims must be examined with, and thus are considered part of, the invention elected. When all claims directed to the elected invention are allowable, should any linking claim be allowable, the restriction requirement between the linked inventions must be withdrawn. Any claim(s) directed to the nonelected invention(s), previously withdrawn from consideration, which depends from or requires all the limitations of the allowable linking claim must be rejoined and will be fully examined for patentability." Id.

Applicant does not traverse the Requirement for Election of Species on the grounds of lack of patentable distinctness between the species. Rather, Applicant traverses the Requirement for Election of Species on the grounds that the relatedness of the species precludes the requirement for election, notwithstanding possible patentable distinctness between the species.

Moreover, Applicant respectfully submits that at least one generic claim as defined above is allowable, and Applicant is then entitled to the consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 C.F.R. § 1.141.

The period for response has been extended until September 16, 2011 by the filing of a request for a two-month extension of time under 37 C.F.R. § 1.136(a) and the payment of the required fee of $245.00 (small entity). The period for response is thereby extended until September 16, 2011. Accordingly, this response is being filed in a timely manner.

V. CONCLUSION

In summary, in response to the Restriction Requirement, Applicant elects the invention of Group I, claims 1-8, 16-21, 25-26, 40-41, 49, 57, 65, 73, 84, and 92, for prosecution on the merits, with traverse. The Examiner is respectfully requested to withdraw the Restriction Requirement.

In response to the Requirement for Election of Species, Applicant elects the following species, all with traverse: (1) for claim 2, non-selective inverse agonists having inverse agonist activity against both β_1 and β_2-adrenergic receptors; (2) for claim 4, nadolol as the β-adrenergic inverse agonist; (3) For claim 5, nadolol as the β-adrenergic inverse agonist; (4) for claim 7, carvedilol as the β-adrenergic inverse agonist; (5) for claim 16, inhalation as a

route of administration; (6) for claim 18, chronic pulmonary obstructive disease as a pulmonary airway disease; (7) for claims 40-41, salbutamol as the β_2-selective adrenergic agonist; (8) for claim 49, prednisone as the steroid; (9) for claim 57, ipratropium bromide as the anticholinergic compound; (10) for claim 65, theophylline as the xanthine compound; (11) for claim 73, a monoclonal antibody as the anti-IgE antibody; (12) for claim 84, ibudilast as the leukotriene modifier; and (13) for claim 92, roflumilast as the phosphodiesterase IV inhibitor.

If any issues remain, the Examiner is respectfully requested to telephone the undersigned at (760) 918-5744.

Respectfully submitted,

Date: September 16, 2011

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